

In the Claims

Please amend the previously submitted Claims 1-37 and please also enter newly added claims 38-42 as follows:

1. (Currently Amended) ~~A variant protein comprising an~~ An Fc variant of a wild-type parent Fc polypeptide, said Fc variant comprising at least one amino acid modification in the Fc region of said ~~wild-type parent Fc~~ polypeptide said modification occurring at a position selected from the group consisting of: 228, 230, 231, 232, 240, 244, 245, 247, 262, 263, 266, 271, 273, 275, 281, 284, 291, 299, 302, 304, 313, 323, 325, 328, 332, and 336, wherein said Fc variant protein exhibits altered binding to an FcγR as compared to the ~~wild-type parent Fc~~ polypeptide, wherein numbering is according to the EU index.
2. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 1, wherein said Fc variant comprises at least one substitution ~~at a position corresponding to an Fc position~~ selected from the group consisting of: 230, 240, 244, 245, 247, 262, 263, 266, 273, 275, 299, 302, 313, 323, 325, 328, and 332.
3. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 1, wherein said altered binding is an increase in affinity of said Fc variant to said FcγR.
4. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein said Fc variant binds with greater affinity to a mouse FcγR.
5. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein said said FcγR is a human Fc receptor selected from the group consisting of FcγRI, FcγRIIa, FcγRIIb, FcγRIIc, and FcγRIIIa.
6. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein said Fc variant binds with greater affinity to human FcγRI and FcγRIIIa, but exhibits unaltered affinity to a human receptor selected from the group consisting of FcγRIIa, FcγRIIb, and FcγRIIc.
7. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 6, wherein said Fc variant exhibits unaltered affinity to FcγRIIa, FcγRIIb, and FcγRIIc.

8. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein the affinity increase for binding to one or more human FcγRII's is greater than the affinity increase for binding to human FcγRI ~~and or~~ FcγRIIIa.
9. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein the affinity increase is the same for binding to FcγRIIIa, FcγRIIb, and FcγRIIc.
10. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim ~~9-3~~, wherein the affinity increase for binding to FcγRIIc is greater than the affinity increase for binding to FcγRIIb.
11. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 3, wherein said Fc variant binds with greater affinity to human FcγRIIIa, but exhibits unaltered affinity to a human receptor selected from the group consisting of FcγRI, FcγRIIb, FcγRIIc, and FcγRIIIa.
12. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 11, wherein said said Fc variant exhibits unaltered affinity to FcγRI, FcγRIIb, FcγRIIc, and FcγRIIIa.
13. (Currently Amended) ~~A variant protein~~ An Fc variant according to any of claims 1-12, wherein said Fc variant binds with greater affinity to FcRn.
14. (Currently Amended) ~~A variant protein~~ An Fc variant according to any of claims 1-12, wherein said Fc variant binds with unaltered affinity to FcRn.
15. (Currently Amended) ~~A variant protein~~ An Fc variant according to any of claims 1-12, wherein said Fc variant binds with reduced affinity to FcRn.
16. (Currently Amended) ~~A variant protein~~ An Fc variant according to any of claims 1-12, wherein said Fc variant binds with greater affinity to C1q or enhances CDC.
17. (Currently Amended) ~~A variant protein~~ An Fc variant according to any of claims 1-12, wherein said Fc variant binds with unaltered affinity to C1q or enhances CDC.
18. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 1, wherein said Fc variant further comprises an engineered glycoform.

19. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 18 wherein said engineered glycoform comprises an altered level of fucosylation or bisecting oligosaccharides as compared to the parent Fc polypeptide.
20. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 18 wherein said engineered glycoform improves effector function.
21. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 1, comprising an Fc variant of a wild-type Fc polypeptide, said Fc variant comprising at least one amino acid modification in the Fc region of said wild-type parent Fc polypeptide, wherein said Fc variant modulates effector function as compared to the parent Fc polypeptide.
22. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 21, wherein said effector function is ADCC.
23. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 22, wherein said Fc variant improves ADCC in the presence of human effector cells as compared to said ~~wild-type parent~~ parent Fc polypeptide.
24. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 22, wherein said ADCC improvement is an enhancement in potency such that the EC50 of said Fc variant is approximately 5-fold greater than that of said parent Fc polypeptide.
25. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 23, wherein said ADCC improvement is an enhancement in potency such that the EC50 of said Fc variant is between approximately 5-fold and 1000-fold greater than that of said parent Fc polypeptide.
26. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 23, wherein said ADCC improvement is an enhancement in efficacy such that the maximal ADCC is approximately 2-fold greater than that of said parent Fc polypeptide.
27. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 26, wherein said Fc variant improves ADCC in the presence of mouse effector cells as compared to said ~~wild-type parent~~ parent Fc polypeptide.
28. (Currently Amended) ~~A variant protein~~ An Fc variant according to claim 21, wherein said effector function is ADCC.

29. (Currently Amended) A-variant-protein An Fc variant according to claim 28, wherein said Fc variant improves ADCP as compared to said wild-type parent Fc polypeptide.
30. (Currently Amended) A-variant-protein An Fc variant according to claim 25 or 29, wherein CDC is unaffected.
31. (Currently Amended) A-variant-protein An Fc variant according to claim 25 or 29, wherein CDC is ablated.
32. (Currently Amended) A-variant-protein An Fc variant according to claim 4 that wherein said polypeptide has specificity for a target antigen selected from the group consisting of CD4, CD19, CD20, CD22, CD25, CD30, CD33, CD52, CD80, B7-1, B7-2, CLTA-4, BAFF-R, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
33. (Currently Amended) A-variant-protein An Fc variant according to claim 1 or 21 comprising a modification selected from the group consisting of 221K, 221Y, 222E, 222Y, 223K, 224E, 224Y, 225E, 225K, 225W, 228E, 228K, 228Y, 228G, 230E, 230Y, 230G, 231E, 231K, 231Y, 231P, 231G, 232E, 232K, 232Y, 232G, 262E, 262F, 271D, 271E, 271N, 271Q, 271K, 271R, 271S, 271T, 271H, 271A, 271V, 271L, 271I, 271F, 271M, 271Y, 271W, 271G, 275L, 281D, 281K, 281Y, 281P, 284E, 284N, 284T, 284L, 284Y, 291D, 291E, 291Q, 291T, 291H, 291I, 291G, 299D, 299E, 299N, 299Q, 299K, 299R, 299L, 299F, 299M, 299Y, 299W, 299P, 299G, 304D, 304N, 304T, 304H, 304L, 325K, 325R, 325S, 325F, 325M, 325Y, 325W, 325P, 325G, 328D, 328Q, 328K, 328R, 328S, 328T, 328V, 328I, 328Y, 328W, 328P, 328G, 332K, 332R, 332S, 332V, 332L, 332F, 332M, 332W, 332P, 332G, 336E, 336K, 336Y, 230A, 240A, 240I, 240M, 240T, 244H, 245A, 247G, 247V, 262A, 262E, 262I, 262T, 263A, 263I, 263M, 263T, 266A, 266I, 266M, 266T, 273I, 275W, 299A, 299E, 299F, 299H, 299I, 299L, 299S, 299V, 302I, 313F, 323I, 325A, 325D, 325E, 325H, 325I, 325L, 325Q, 325T, 325V, 328A, 328D, 328E, 328F, 328H, 328I, 328M, 328N, 328Q, 328T, 328V, 332A, 332D, 332E, 332H, 332N, 332Q, 332T, and 332Y –239D, 239E, 239N, 239Q, 239T, 240I, 240M, 264I, 264T, 264Y, 297D, 330I, 330L, 330Y, 332D, 332E, 332N, 332Q, A231E, A231G, A231K, A231P, A231Y, A298H, A327D, A327E, A327F, A327H, A327I, A327K, A327L, A327M, A327N, A327P, A327R, A327T, A327T, A327V, A327W, A327Y, A330E, A330F, A330F, A330G, A330H, A330I, A330L, A330L/I332E, A330M, A330N, A330P, A330R, A330S, A330T, A330V, A330W, A330Y, A330Y, A330Y/I332E, D221K, D221Y, D249H, D249Q, D249Y, D265F, D265F/N297E/I332E, D265G, D265H, D265I, D265K, D265L, D265M, D265N, D265P, D265Q, D265R, D265S, D265T, D265V, D265W, D265Y, D265Y/N297D/I332E, D265Y/N297D/T299L/I332E, D270F, D270G, D270H, D270I, D270L, D270M, D270P, D270Q, D270R, D270S, D270T, D270W, D270Y, D280G, D280H, D280K, D280L, D280P, D280Q, D280W, D280Y, E233A, E233D, E233F, E233G, E233H, E233I, E233K, E233L, E233M, E233N, E233Q, E233R, E233S, E233T, E233V, E233W, E233Y, E258H, E258S, E258Y, E260F, E260G, E260H, E260I, E260K, E260L, E260M, E260N, E260P, E260R, E260S, E260T, E260V, E260W, E260Y, E272D, E272F, E272G, E272H, E272I, E272K, E272L, E272M, E272P, E272R, E272S, E272T, E272V, E272W, E272Y, E283G, E283H, E283K, E283L, E283P, E283R, E283Y, E293F, E293G, E293H, E293I, E293L, E293M, E293N, E293P, E293R, E293S, E293T, E293V, E293W, E293Y, E294F, E294G, E294H, E294I, E294K, E294L, E294M, E294N, E294P, E294R, E294S, E294T, E294V, E294W, E294Y, E318H, E318L, E318Q, E318R, E318Y, E333A, E333F, E333H, E333I, E333L, E333M, E333P, E333S, E333T, E333Y, F241D, F241E, F241E/F243Q/V262T/V264E, F241E/F243Q/V262T/V264E/I332E, F241E/F243R/V262E/V264R, F241E/F243R/V262E/V264R/I332E, F241E/F243Y/V262T/V264R, F241E/F243Y/V262T/V264R/I332E, F241L, F241L/F243L/V262I/V264I, F241L/V262I, F241R, F241E/F243Y/V262T/V264R/I332E, F241R/F243Q/V262T/V264R/I332E, F241W, F241W/F243W,

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33. (Currently Amended) A variant protein An Fc variant according to claim 1 or 24 wherein said variant protein parent Fc polypeptide is an antibody comprising said Fc variant.
34. (Currently Amended) A variant protein An Fc variant according to claim 1 or 24 wherein said Fc variant protein is an Fc fusion protein comprising said Fc variant.
36. (Currently Amended) A pharmaceutical composition comprising a an Fc variant protein according to claim 1 and a pharmaceutically acceptable carrier.
37. (Withdrawn) A method of treating a mammal in need of said treatment, comprising administering a variant protein of claim 1.
38. (New) An Fc variant according to claims 1 or 33 comprising at least one modification selected from the group consisting of A330L/I332E, D265F/N297E/I332E, D265Y/N297D/I332E, D265Y/N297D/T299L/I332E, F241E/F243Q/V262T/V264E, F241E/F243Q/V262T/V264E/I332E, F241E/F243R/V262E/V264R, F241E/F243R/V262E/V264R/I332E, F241E/F243Y/V262T/V264R, F241E/F243Y/V262T/V264R/I332E, F241L/F243L/V262I/V264I, F241L/V262I, F241R/F243Q/V262T/V264R, F241R/F243Q/V262T/V264R/I332E, F241W/F243W/V262A/V264A, F241Y/F243Y/V262T/V264T, F241Y/F243Y/V262T/V264T/N297D/I332E, F243L/V262I/V264W, F243L/V264I, L328D/I332E, L328E/I332E, L328H/I332E, L328I/I332E, L328M/I332E, L328N/I332E, L328Q/I332E, L328T/I332E, L328V/I332E, N297D/A330Y/I332E, N297D/I332E, N297D/I332E/S239D/A330L, N297D/S298A/A330Y/I332E, N297D/T299E/I332E, N297D/T299F/I332E, N297D/T299H/I332E, N297D/T299I/I332E, N297D/T299L/I332E, N297D/T299V/I332E, N297E/I332E, N297S/I332E, P230A/E233D/I332E, P244H/P245A/P247V, S239D/A330L/I332E, S239D/A330Y/I332E, S239D/A330Y/I332E/K326E, S239D/A330Y/I332E/K326T,

S239D/A330Y/I332E/L234I, S239D/A330Y/I332E/L235D, S239D/A330Y/I332E/V240I, S239D/A330Y/I332E/V264T, S239D/A330Y/I332E/V266I, S239D/D265F/N297D/I332E, S239D/D265H/N297D/I332E, S239D/D265I/N297D/I332E, S239D/D265L/N297D/I332E, S239D/D265T/N297D/I332E, S239D/D265V/N297D/I332E, S239D/D265Y/N297D/I332E, S239D/I332D, S239D/I332E, S239D/I332E/A330I, S239D/I332N, S239D/I332Q, S239D/N297D/I332E, S239D/N297D/I332E/A330Y, S239D/N297D/I332E/A330Y/F241S/F243H/V262T/V264T, S239D/N297D/I332E/K326E, S239D/N297D/I332E/L235D, S239D/S298A/I332E, S239D/V264I/A330L/I332E, S239D/V264I/I332E, S239D/V264I/S298A/I332E, S239E/D265N, S239E/D265Q, S239E/I332D, S239E/I332E, S239E/I332N, S239E/I332Q, S239E/N297D/I332E, S239E/V264I/A330Y/I332E, S239E/V264I/I332E, S239E/V264I/S298A/A330Y/I332E, S239N/A330L/I332E, S239N/A330Y/I332E, S239N/I332D, S239N/I332E, S239N/I332N, S239N/I332Q, S239N/S298A/I332E, S239Q/I332D, S239Q/I332E, S239Q/I332N, S239Q/I332Q, S239Q/V264I/I332E, S298A/I332E, V264E/N297D/I332E, V264I/A330L/I332E, V264I/A330Y/I332E, V264I/I332E, V264I/S298A/I332E, Y296D/N297D/I332E, Y296E/N297D/I332E, Y296H/N297D/I332E, Y296N/N297D/I332E, Y296Q/N297D/I332E, and Y296T/N297D/I332E.

39. (New) An Fc variant according to claims 1, 33 or 38 further comprising a modification selected from the group consisting of 227E, 227K, 227Y, 227G, 233N, 233Q, 233K, 233R, 233S, 233T, 233H, 233A, 233V, 233L, 233I, 233F, 233M, 233Y, 233W, 233G, 234K, 234R, 234S, 234A, 234M, 234W, 234P, 234G, 235E, 235K, 235R, 235A, 235M, 235W, 235P, 235G, 236D, 236E, 236N, 236Q, 236K, 236R, 236S, 236T, 236H, 236A, 236V, 236L, 236I, 236F, 236M, 236Y, 236W, 236P, 237D, 237E, 237N, 237Q, 237K, 237R, 237S, 237T, 237H, 237V, 237L, 237I, 237F, 237M, 237Y, 237W, 237P, 238D, 238E, 238N, 238Q, 238K, 238R, 238S, 238T, 238H, 238V, 238L, 238I, 238F, 238M, 238Y, 238W, 238G, 239Q, 239K, 239R, 239V, 239L, 239I, 239M, 239W, 239P, 239G, 241D, 241E, 241Y, 243E, 246D, 246E, 246H, 246Y, 249Q, 249H, 249Y, 255E, 255Y, 258S, 258H, 258Y, 260D, 260E, 260H, 260Y, 264D, 264E, 264N, 264Q, 264K, 264R, 264S, 264H, 264W, 264P, 264G, 265Q, 265K, 265R, 265S, 265T, 265H, 265V, 265L, 265I, 265F, 265M, 265Y, 265W, 265P, 267E, 267Q, 267K, 267R, 267V, 267L, 267I, 267F, 267M, 267Y, 267W, 267P, 268D, 268E, 268Q, 268K, 268R, 268T, 268V, 268L, 268I, 268F, 268M, 268W, 268P, 268G, 269K, 269S, 269V, 269I, 269M, 269W, 269P, 269G, 270R, 270S, 270L, 270I, 270F, 270M, 270Y, 270W, 270P, 270G, 272D, 272R, 272T, 272H, 272V, 272L, 272F, 272M, 272W, 272P, 272G, 274D, 274N, 274S, 274H, 274V, 274I, 274F, 274M, 274W, 274P, 274G, 276D, 276T, 276H, 276V, 276I, 276F, 276M, 276W, 276P, 276G, 278D, 278N, 278Q, 278R, 278S, 278H, 278V, 278L, 278I, 278M, 278P, 278G, 280K, 280L, 280W, 280P, 280G, 282E, 282K, 282Y, 282P, 282G, 283K, 283H, 283L, 283Y, 283P, 283G, 285D, 285E, 285Q, 285K, 285Y, 285W, 286E, 286Y, 286P, 286G, 288D, 288E, 288Y, 290D, 290N, 290H, 290L, 290W, 292D, 292E, 292T, 292Y, 293N, 293R, 293S, 293T, 293H, 293V, 293L, 293I, 293F, 293M, 293Y, 293W, 293P, 293G, 294K, 294R, 294S, 294T, 294H, 294V, 294L, 294I, 294F, 294M, 294Y, 294W, 294P,

294G, 295D, 295E, 295N, 295R, 295S, 295T, 295H, 295V, 295I, 295F, 295M, 295Y, 295W, 295P, 295G, 296K, 296R, 296A, 296V, 296M, 296G, 297Q, 297K, 297R, 297T, 297H, 297V, 297L, 297I, 297F, 297M, 297Y, 297W, 297P, 297G, 298D, 298E, 298Q, 298K, 298R, 298I, 298F, 298M, 298Y, 298W, 300D, 300E, 300N, 300Q, 300K, 300R, 300S, 300T, 300H, 300A, 300V, 300M, 300W, 300P, 300G, 301D, 301E, 301H, 301Y, 303D, 303E, 303Y, 305E, 305T, 305Y, 317E, 317Q, 318Q, 318H, 318L, 318Y, 320N, 320S, 320H, 320V, 320L, 320F, 320Y, 320W, 320P, 320G, 322D, 322S, 322V, 322I, 322F, 322Y, 322W, 322P, 322G, 324H, 324F, 324M, 324W, 324P, 324G, 326P, 327E, 327K, 327R, 327H, 327V, 327I, 327F, 327M, 327Y, 327W, 327P, 329D, 329E, 329N, 329Q, 329K, 329R, 329S, 329T, 329H, 329V, 329L, 329I, 329M, 329Y, 329W, 329G, 330E, 330N, 330T, 330P, 330G, 331D, 331Q, 331R, 331T, 331L, 331I, 331F, 331M, 331Y, 331W, 333L, 333F, 333M, 333P, 334P, 335N, 335S, 335H, 335V, 335L, 335I, 335F, 335M, 335W, 335P, 335G, 337E, 337N, 337H, 233D, 234D, 234E, 234F, 234H, 234I, 234N, 234Q, 234T, 234V, 234Y, 235D, 235F, 235H, 235I, 235N, 235Q, 235S, 235T, 235V, 235Y, 239D, 239E, 239F, 239H, 239N, 239Q, 239T, 239Y, 241E, 241L, 241R, 241S, 241W, 241Y, 243H, 243L, 243Q, 243R, 243W, 243Y, 264A, 264E, 264F, 264I, 264L, 264M, 264R, 264T, 264W, 264Y, 265F, 265G, 265H, 265I, 265L, 265N, 265Q, 265T, 265V, 265Y, 267D, 267H, 267L, 267N, 267Q, 267T, 269F, 269H, 269L, 269N, 269R, 269T, 269Y, 270H, 270Q, 270T, 272I, 272K, 272S, 272Y, 274E, 274L, 274R, 274T, 274Y, 276E, 276L, 276R, 276S, 276Y, 278E, 278K, 278T, 278W, 283R, 296D, 296E, 296H, 296I, 296L, 296N, 296Q, 296S, 296T, 297D, 297E, 297S, 298A, 298H, 298N, 298T, 318R, 320D, 320I, 320T, 322H, 322T, 324D, 324I, 324L, 324R, 324T, 324V, 324Y, 326E, 326I, 326L, 326T, 327D, 327L, 327N, 327S, 327T, 329F, 330F, 330H, 330I, 330L, 330M, 330R, 330S, 330V, 330W, 330Y, 331H, 331V, 333A, 333H, 333I, 333T, 333Y, 334A, 334F, 334I, 334T, 335D, 335R, and 335Y.

40. (New) An Fc variant according to claim 1 wherein said Fc variant further comprises a set of modifications selected from 241W/243W, 267Q/327S, 243L/264I, 234I/235D, 264E/297D/332E, 239E/265N, 239E/265Q, 239E/265G, 267L/327S and 240I/266I.

41. (New) An Fc variant according to claim 33 wherein said antibody is a full length antibody.

41. (New) An Fc variant according to claim 33 wherein said antibody is a human antibody.

42. (New) An Fc variant according to claim 33 wherein said antibody is an antibody fragment.